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## NOTICE OF ALLOWANCE AND FEE(S) DUE

32793 7590 07/03/2008

TAKEDA SAN DIEGO, INC.  
10410 SCIENCE CENTER DRIVE  
SAN DIEGO, CA 92121

EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 07/03/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,011	06/20/2003	Ciaran N. Cronin	SYR-AIK-5001-C1	5098

TITLE OF INVENTION: CRYSTALLIZATION OF AURORA/PLIP-RELATED KINASE

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$720	\$0	\$0	\$720	10/03/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS** FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

## HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to:** **Mail** **Mail Stop ISSUE FEE**  
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**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

32793 7590 07/03/2008  
**TAKEDA SAN DIEGO, INC.**  
**10410 SCIENCE CENTER DRIVE**  
**SAN DIEGO, CA 92121**

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,011	06/20/2003	Ciaran N. Cronin	SYR-AIK-5001-C1	5098

**TITLE OF INVENTION:** CRYSTALLIZATION OF AURORA/PLIP-RELATED KINASE

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nonprovisional	YES	\$720	\$0	\$0	\$720	10/03/2008

EXAMINER	ART UNIT	CLASS-SUBCLASS
STEADMAN, DAVID J	1656	702-011000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB-122) attached.  
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB-47; Rev 03-02 or more recent) attached. Use of a **Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_  
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_  
3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

**PLEASE NOTE:** Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee  
☐ Publication Fee (No small entity discount permitted)  
☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.  
☐ Payment by credit card. Form PTO-2038 is attached.  
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

**NOTE:** The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_ Date \_\_\_\_\_  
Typed or printed name \_\_\_\_\_ Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.**

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10/601,011	06/20/2003	Ciaran N. Cronin	SYR-AIK-5001-C1	5098
32793	7590	07/03/2008	EXAMINER	
TAKEDA SAN DIEGO, INC. 10410 SCIENCE CENTER DRIVE SAN DIEGO, CA 92121			STEADMAN, DAVID J	
			ART UNIT	PAPER NUMBER

1656

DATE MAILED: 07/03/2008

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 249 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 249 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

**Notice of Allowability****Application No.**

10/601,011

**Applicant(s)**

CRONIN ET AL.

**Examiner**

David J. Steadman

**Art Unit**

1656

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendment filed on 4/21/08.
2. ☒ The allowed claim(s) is/are 1,4,9,12,15,17,27-29,31,34 and 36.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of the:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.  
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached  
1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.  
(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.  
**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_.

**DETAILED ACTION**

***Status of the Application***

[1] Claims 1, 4, 9, 12, 15, 17, 27-29, 31, 34, and 36 are pending in the application following the examiner's amendment as set forth below.

[2] Applicant's amendment to the claims, filed on 4/21/08, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims. Claims 1, 9, and 29 are amended and claims 32-33 have been canceled relative to the claim set filed on 10/15/07.

[3] Applicant's arguments filed on 4/21/08 in response to the Office action mailed on 12/19/07 are acknowledged. Applicant's arguments have been fully considered and in combination with the claim amendment filed on 4/21/08 and the examiner's amendment to the claims as set forth below are deemed to be persuasive to overcome the rejection(s) and objection(s) previously applied.

***Election/Restriction***

[4] Examined claim 27-29 correspond to non-elected claims 18 and 22-23, but differ from claims 18 and 22-23 in that they include all the limitations of allowed claims 9 and 15 and are commensurate in scope with the allowed claims 9 and 15. The restriction requirement between Groups I and II as set forth in the restriction requirement mailed on 12/2/05 has been withdrawn. Because claims 18 and 22-25 are not commensurate in scope with the allowed claims, these claims have not been rejoined with the claims of

the elected invention and, as noted below, applicant has agreed to cancel these withdrawn claims by examiner's amendment.

[5] In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

#### ***Examiner's Amendment to the Specification***

[6] An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Lekha Gopalakrishnan on 7/1/08.

[7] The application has been amended as follows:

[8] Please replace paragraph [0010] at p. 2 of the specification with the following re-written paragraph: "In one variation, the protein crystal has a crystal lattice in a P6<sub>3</sub>22 space group. The protein crystal may also have a crystal lattice having unit cell

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dimensions, +/- 5%, of  $a=80.45\text{\AA}$ ,  $b=80.45\text{\AA}$  and  $c=172.18\text{\AA}$ . The protein crystal may also have a crystal lattice having unit cell dimensions, +/- 2%, of  $a=80.45\text{\AA}$ ,  $b=80.45\text{\AA}$  and  $c=172.18\text{\AA}$ .

[9] The above amendment is made in accordance with 37 CFR 1.75(d)(1) and MPEP § 608.01(o) to provide antecedent basis in the specification for the limitation of "+/- 2%" variability in the unit cell dimensions, as set forth in the examiner's amendment below. This examiner's specification and claim amendment are supported by provisional application 60/390,355, to which this application claims priority under 35 U.S.C. 119(e). See, e.g., p. 2, lines 25-28 and p. 3, lines 10-14 of the 60/390,355 provisional application. According to the specification's continuing data at p. 1, paragraph [001], the 60/390,355 provisional has been properly incorporated by reference.

***Examiner's Amendment to the Claims***

[10] An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in telephone interviews with Ms. Lekha Gopalakrishnan on 6/25/08 and 6/30/08.

[11] The application has been amended as follows:

[12] Cancel claims 18, 22-25, 30, and 35.

[13] In claims 1 and 9, replace "+/-5%" with "+/-2%".

**[14]** In claim 27, insert ---potentially--- after "that" in line 3.

***Reasons for Allowance***

**[15]** The following is an Examiner's statement of reasons for allowance. Residues 29-295 of SEQ ID NO:3 are a fragment of Aurora kinase and residues 24-28 of SEQ ID NO:3 are a non-naturally-occurring artifact of cleavage by rTEV protease. Residues 1-23 of SEQ ID NO:3 has a histidine tag to facilitate purification and additionally has an rTEV protease cleavage site between residues 23 and 24 of SEQ ID NO:3. See particularly specification at p. 47, paragraph 196 and Figure 1.

Claim 1 recites a crystal complexed with a "ligand that is bound to the ATP binding site of the protein" and claim 9 recites a crystal in complex with "an ATP binding site ligand". Such crystals are enabled because given the exact protein sequence and space group and unit cell parameters, the variables for which one skilled in the art would have to screen for is simplified to one, e.g. the ATP-binding site ligand, which is reasonable and would not necessitate any undue experimentation. Given that crystallizing any proteins can be extremely unpredictable, the protein as recited in the instant claims has been fully described and enabled, because of the noted considerable detail of precise protein sequence, space group and unit cell parameters, and the disclosed crystallization conditions. Finally, the recited genus of ATP-binding site ligands is described as ATPyS is deemed to be representative of the ligands that would fit into this binding site either by co-crystallization or by replacement of ATPyS through simple soaking of the ligand with the formed crystals.



Claims 17, 31, 34, and 36 are drawn to a "non-crystalline" polypeptide. In analyzing the specification's descriptive support for the limitation of "non-crystalline", it is noted that according to MPEP 2173.05(i), "Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977)". See also the Court's holding in *Ex parte Parks*, 30 USPQ2d 1234 (Bd. Pat. App. & Int. 1993), "[i]n rejecting a claim under the first paragraph of 35 U.S.C. 112 for lack of adequate descriptive support, it is incumbent upon the examiner to establish that the originally-filed disclosure would not have reasonably conveyed to one having ordinary skill in the art that an appellant had possession of the now claimed subject matter. *Wang Laboratories, Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed.Cir. 1993). Adequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention. *In re Herschler*, 591 F.2d 693, 200 USPQ 711 (CCPA 1979); *In re Edwards*, 568 F.2d 1349, 196 USPQ 465 (CCPA 1978; *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed. *In re Anderson*, 471 F.2d 1237, 176 USPQ 331 (CCPA 1973)."

In this case, while there does not appear to be *in haec verba* support for the limitation of "non-crystalline" in the specification, it is noted that the specification discloses "crystal" or "crystalline" polypeptides as encompassed by the claims and

further, the specification throughout contemplates the polypeptides encompassed by the claims in a non-crystalline form, *i.e.*, solution form. Moreover, one of skill in the art would recognize that in order to crystallize the polypeptides, one must necessarily first produce them in a solution or non-crystalline form. As such, it is the examiner's position that the limitation of "non-crystalline" finds adequate descriptive support in the original application as filed.

Also, there does not appear to be *in haec verba* support for the limitation of the range of amino acids 24-295 of SEQ ID NO:3 in the original application. However, as noted in a prior Office action, it was well-known at the time of the invention that recombinant TEV (rTEV) protease cleaves at a Glu-Asn-Leu-Tyr-Phe-Gln\*Gly recognition site. See particularly the reference of Polayes et al. (*Life Technology Focus* 18:2-5; filed on 9/4/07) at p. 2, column 1. As SEQ ID NO:3 has such a recognition site at amino acids 18-24 and the specification expressly teaches (p. 47, paragraph 196), "...the polyhistidine tags [of SEQ ID NO:3] may optionally be removed by treatment with rTEV protease...In this instance, the polyhistidine tag was removed", a skilled artisan would immediately recognize that cleavage of SEQ ID NO:3 by rTEV protease as disclosed in the specification at p. 47, paragraph 196 would remove the first 23 amino acids of SEQ ID NO:3, resulting in a polypeptide with an N-terminal deletion of the first 23 amino acids of SEQ ID NO:3. Since SEQ ID NO:3 is a 295 amino acid polypeptide, the resulting polypeptide would necessarily be amino acids 24-295 of SEQ ID NO:3.

In this case, the examiner can find no teaching in the prior art of record of the polypeptide of SEQ ID NO:3, the polypeptide of residues 24-295 of SEQ ID NO:3 or

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crystals thereof as encompassed by the claims, and methods for making such crystals. Therefore, claims 1, 4, 9, 12, 15, 17, 27-29, 31, 34, and 36, drawn to the polypeptide of SEQ ID NO:3, the polypeptide of residues 24-295 of SEQ ID NO:3 and crystals thereof as encompassed by the claims, and methods for making such crystals are allowable over the prior art of record.

**[16]** Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Steadman/  
David J. Steadman, Ph.D.  
Primary Examiner  
Art Unit 1656